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09/994,466	11/26/2001	Ragupathy Madiyalakan	AREX-P03-002	7223
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ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			HUFF, SHEELA JITENDRA	
			ART UNIT	PAPER NUMBER
			1642	

DATE MAILED: 05/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

# Office Action Summary

Application No.

09/994,466

Applicant(s)

MADIYALAKAN, RAGUPATHY

Examiner

Sheela J Huff

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

## Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

## Status

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

## Disposition of Claims

- 4) ☒ Claim(s) 1-41 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-41 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

## Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

## Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

## Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_.

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### **DETAILED ACTION**

Claims 1-41 are pending.

Applicant is requested to update the priority information found on the first page of the specification.

#### ***Information Disclosure Statement***

The IDS filed 2/24/03 and 3/24/03 have been considered and initialed copies of the PTO-1449 are enclosed.

#### ***Claim Rejections - 35 USC § 112***

Claims 1-15, 22 and 35-37 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure without complete evidence either that the claimed biological materials are known and readily available to the public or complete evidence of the deposit of the biological materials.

The specification lacks complete deposit information for the deposit of hybridoma cell line producing Alt-1. It is not clear that aforementioned hybridoma possessing the identical properties of the hybridoma producing Alt-1 are known and publicly available or can be reproducibly isolated from nature without undue experimentation.

Exact replication of a cell line is an unpredictable event. Although applicant has provided a written description of a method for selecting the claimed hybridoma cell lines and monoclonal antibodies, this method will not necessarily reproduce antibodies and hybridomas which are chemically and structurally identical to those claimed. It is unclear that one of skill in the art could derive a monoclonal antibody and hybridoma identical to those claimed. Undue experimentation would be required to screen all of the possible antibody and hybridoma species to obtain the claimed antibodies and hybridomas.

Because one of ordinary skill in the art could not be assured of the ability to practice the invention as claimed in the absence of the availability of the claimed hybridoma, a suitable deposit for patent purposes, evidence of public availability of the

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claimed hybridoma or evidence of the reproducibility without undue experimentation of the claimed hybridoma, is required.

Applicant's referral to the deposit of Alt-1 on page 10, line 26 of the specification is an insufficient assurance that the required deposit has been made and all the conditions of 37 CFR 1.801-1.809 met.

If the deposit is made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicant or assignees or a statement by an attorney of record who has authority and control over the conditions of deposit over his or her signature and registration number stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty and that all restrictions upon public access to the deposited material will be irrevocably removed upon the grant of a patent on this application. This requirement is necessary when deposits are made under the provisions of the Budapest Treaty as the Treaty leaves this specific matter to the discretion of each State.

If the deposit is not made under the provisions of the Budapest Treaty, then in order to certify that the deposits comply with the criteria set forth in 37 CFR 1.801-1.809 regarding availability and permanency of deposits, assurance of compliance is required. Such assurance may be in the form of an affidavit or declaration by applicants or assignees or in the form of a statement by an attorney of record who has the authority and control over the conditions of deposit over his or her signature and registration number averring:

(a) during the pendency of this application, access to the deposits will be afforded to the Commissioner upon request:

(b) all restrictions upon the availability to the public of the deposited biological material will be irrevocably removed upon the granting of a patent on this application:

(c) the deposits will be maintained in a public depository for a period of at least thirty years from the date of deposit or for the enforceable life of the patent or for a period of five years after the date of the most recent request for the furnishing of a sample of the deposited biological material, whichever is longest; and

(d) the deposits will be replaced if they should become nonviable or non-replicable.

Amendment of the specification to recite the date of deposit and the complete name and address of the depository is required. As an additional means for completing the record, applicant may submit a copy of the contract with the depository for deposit and maintenance of each deposit.

If a deposit is made after the effective filing date of the application for patent in the United States, a verified statement is required from a person in a position to corroborate that the biological material described in the specification as filed is the same as that deposited in the depository, stating that the deposited material is identical to the biological material described in the specification and was in the applicant's possession at the time the application was filed.

Applicant's attention is directed to *In re Lundak*, 773 F.2d. 1216, 227 USPQ 90 (CAFC 1985) and 37 CFR 1.801-1.809 for further information concerning deposit practice.

Claims 16-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the use of Alt-1 to treat a tumor wherein the mammal generates an immune response that comprises an antibody that specifically binds to an epitope of tumor-associated MUC1 that is different from the epitope of tumor associated MUC1 that is specifically bound by Alt-1, does not reasonably provide enablement for the use of any binding agent to treat a tumor wherein the mammal generates an immune response that comprises an antibody that specifically binds to an epitope of tumor-associated MUC1 that is different from the epitope of tumor associated MUC1 that is specifically bound by the binding agent. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure meets the enablement requirement of 35 USC 112, first paragraph, have been described in *In Re Colianni*, 195 USPQ 150 (CCPA 1977) and have been adopted by the Board of Patent

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Appeals and Interferences in Ex Parte Forman, 230 USPQ 546 (BPAI 1986). Among these factors are:

1. the nature of the invention,
2. the state of the prior art,
3. the predictability or lack thereof in the art,
4. the breath of the claims,
5. the amount of direction or guidance present, and
6. the presence or absence of working examples.

The following is an analysis of these factors in relationship to this application.

Applicant claims and discloses the use of any binding agent to generate an immune response that comprises an antibody that specifically binds to an epitope of tumor-associated MUC1 that is different from the epitope of tumor associated MUC1 that is specifically bound by the binding agent. In other words, applicant is claiming that the binding agent activates the anti-idiotypic response and the antibody that applicant claims that binds to a different epitope is Ab3. However, applicant has only shown that this can be achieved with Alt-1 as the agent.

The state of the art that when the anti-idiotypic response is activated the resulting anti-anti-idiotypic antibodies (or Ab3, which is what applicant is generating) react to the same epitope as that of Ab1 (the binding agent in the instant application) (see page 65 of Herlyn et al Cancer Immunol. Immunother (1996) 43:65-76). Applicant is claiming that the epitope recognized by the Ab3 is different than that recognized by Ab1. Chatterjee et al (U.S. Patent 6,235,280 B1) teach that not all anti-idiotypic antibodies can be used in therapeutic regimens against tumors. First, only a fraction of antibodies raised against an Ab1 (anti-antigen antibody) are limited in their reactivity to the paratope of Ab1 (i.e., are non-reactive against features shared with other potential antibodies in the host). Second, anti-idiotypic antibodies are not necessarily

immunogenic. Third, only a fraction of the immunogenic anti-idiotypes elicit an antigen-specific immune response. Further, anti-idiotypic therapy with respect to tumor origin and antigens expressed should be evaluated on a case-by-case basis since different cancers have widely varying molecular and clinical characteristics (see column 2, lines 39-53).

While applicant is effectively shown this for Alt-1, applicant has not shown that any binding agent other than Alt-1 can induce such an anti-idiotypic response. Another important point is that the state of the art discloses immunizing with Ab1 or Ab2. Whereas applicant is not immunizing with Ab2, applicant is merely relying on the Ab2 produced in response to Ab1. Since it is clear from the state of the art that anti-idiotypic antibodies (Ab2) are not necessarily immunogenic and applicant is merely relying on the population of Ab2 produced in the mammal (and not a high concentration of Ab2), the producing of Ab3 would be limited.

In view of the above, it is the Examiner's position that one skilled in the art could not make and/or use the invention without undue experimentation.

Claims 2-3, 9-11, 13 and 33 and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

- a. In claims 2, 9-11, the terminology "the binding agent" has no proper antecedent basis.
- b. Claims 13 is the same as claim 6.

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- c. Claim 33 is improperly depending from a claim recited after claim 33.
- d. Claim 38 uses the terminology "activated" and this renders the claim vague and indefinite. "Activated" by what?

### ***Double Patenting***

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

Claims 35-36 are rejected under 35 U.S.C. 101 as claiming the same invention as that of claim 1-2 of prior U.S. Patent No. 6716966. This is a double patenting rejection.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

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Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 34 and 37 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 and 3 of U.S. Patent No. 6716966. Although the conflicting claims are not identical, they are not patentably distinct from each other because the only difference between the two sets of claims is that the epitope in patent is limited to the sequence DTRPAP and the epitope in the instant application is directed to a peptide comprising said sequence.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 30-32, 34-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Spencer et al Cancer Letters 100(1996) 11-15.

This reference discloses antibody C595 (see entire reference). This anti-MUC antibody recognizes the sequence RPRP (see figure 1). This antibody was used in a composition because it was used in an ELISA assay. It is inherent that the antibody can treat a tumor that expresses a tumor-associated MUC1.

Claims 30, 32, 34-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Spencer et al Cancer Letters 100(1996) 11-15.

This reference discloses antibody HMFG1 (see entire reference). This anti-MUC antibody recognizes the sequence DTRP (see figure 1). This antibody was used in a composition because it was used in an ELISA assay. It is inherent that the antibody can treat a tumor that expresses a tumor-associated MUC1.

Claims 30-32 and 34-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Price et al. Breast 2:3-7 (1993).

This reference discloses antibodies against polymorphic epithelial mucins (PEM) (see entire reference). This reference discloses BC2 and HMFG-2 which bind to a sequence in the APDTRPAP (specific epitopes are given in the Table on page 4). These antibodies have been used in immunoassay (see abstract) (thus reading on composition). The antibody is inherent that the antibody can treat a tumor that expresses a tumor-associated MUC1.

Claims 30, 32-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Price et al. Breast 2:3-7 (1993).

This reference discloses antibodies against polymorphic epithelial mucins (PEM) (see entire reference). This reference discloses anti-PEM antibodies other than HMFG-1 which bind to a sequence in the APDTRPAP (specific epitopes are given in the Table on page 4). These antibodies have been used in immunoassay (see abstract) (thus reading on composition). The antibody is inherent that the antibody can treat a tumor that expresses a tumor-associated MUC1.

Claims 30, 32-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Devine et al BioEssays vol. 14 (1992) pp. 619-625.

This reference discloses antibodies to DF3, Mc1, Mc5, BrE1, HMFG2 and F36/22 and B72.3, SH1 and that these AB have been used in therapeutic application to target and reduce tumor growth (see page 624, first column).

Claims 30-32, 34-35 and 37-38 are rejected under 35 U.S.C. 102(b) as being anticipated by Devine et al BioEssays vol. 14 (1992) pp. 619-625.

This reference discloses antibodies to Mc1, BrE1, HMFG1, and F36/22 and B72.3, SH1 and that these AB have been used in therapeutic application to target and reduce tumor growth (see page 624, first column) and in diagnostic applications (see top of Table 4).

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

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The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Devine et al BioEssays vol. 14 (1992) pp. 619-625 in view of WO 98/33470 and Spencer et al Cancer Letters 100(1996) 11-15 or Price et al. Breast 2:3-7 (1993).

The primary references have been discussed above.

The only difference between the primary references and the instant invention is the use of a photodynamic agent.

WO 98/33470 discloses the use of photodynamic agents, such as hypocrellin, and the advantages of their use in treatment or cancer and diagnosis in cancer when coupled to monoclonal antibodies (see page 3 and entire reference).

Since the primary reference discloses the diagnostic and therapeutic use of anti-muc1 antibodies enhance the diagnostic use of antibodies, it would have been obvious to one of ordinary skill in the art at the time of applicant's invention to use photodynamic agents such as hypocrellin to enhance the diagnostic use of the antibodies of the primary reference. Since all the antibodies of Devine et al, Spencer et al and Price et al are directed to muc1, it would have been within the purview of one skilled in the art to conjugate any of the known ab with a photodynamic agent.

**Conclusion**

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheela J Huff whose telephone number is 571-272-0834. The examiner can normally be reached on Tuesday 5:30am-11:30am and Fridays 6:00am-4:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

  
Sheela J Huff  
Primary Examiner  
Art Unit 1642

sjh